UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/812,508	03/07/1997	JANAK KHIMCHAND PADIA	5117-C1-41-E	2435

28880 7590 08/04/2004

WARNER-LAMBERT COMPANY
2800 PLYMOUTH RD
ANN ARBOR, MI 48105

EXAMINER	
RAO, DEEPAK R	
ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 08/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/812,508	PADIA, JANAK KHIMCHAND	
	Examiner	Art Unit	
	Deepak R Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *73-88* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *76,77,80-83,85 and 86* is/are allowed.

6)☒ Claim(s) *73-75,78,79,84,87 and 88* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to the amendment filed on May 6, 2004.

Claims 73-88 are pending in this application.

The following rejections are withdrawn:

The rejections under 35 U.S.C. 112, second paragraph of the previous office action are rendered moot by cancellation of the previously presented claims.

The rejection under 35 U.S.C. 102(b) over Kottke et al., Chem. Abstract 99:158378h of the previous office action is rendered moot by the cancellation of the previously presented claims.

The following rejections are maintained:

1. Claim 88 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment, does not reasonably provide enablement for prevention of panic. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claim. Reasons provided in the previous office action in the rejection of claims 70 and 72 are incorporated here by reference.

Applicant relies on the amendment to overcome the rejection, however, the newly presented claim 88 continues to recite "an agent for treating or preventing panic".

2. Claims 73-75, 78 and 88 are rejected under 35 U.S.C. 102(b) as being anticipated by DD 225131 (Chem. Abstract 104:207299). The instant claims read on reference disclosed

compounds, see e.g., RN 77747-37-6. The instant claims recite R_1 and R_2 are 'substituted phenyl', however, the substituent list includes hydrogen (as can be seen from claim 78).

Applicant submits that the rejection is obviated by the newly presented claims, however, the claims continue to read on reference compounds.

3. Claims 73-75, 78 and 88 are rejected under 35 U.S.C. 102(b) as being anticipated by DD 158549 (Chem. Abstract 99:70757). The instant claims read on reference disclosed compounds, see e.g., RN 77747-37-6, RN 77775-32-7, RN 85773-41-7, etc. The instant claims recite R_1 and R_2 are 'substituted phenyl', however, the substituent list includes hydrogen (as can be seen from claim 78).

Applicant submits that the rejection is obviated by the newly presented claims, however, the claims continue to read on reference compounds.

The following rejections are under new grounds:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 79, 84 and 87-88 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of gastrointestinal ulcers, does not reasonably provide enablement for (a) method of treating all conditions advantageously affected by the binding of the compound to a CCK receptor (b) method of blocking drug or alcohol withdrawal reaction and (c) method of diagnosis of gastrin-dependent tumors. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations.

The instant claim 79 are drawn to "a method for treating a condition advantageously affected by the binding of the compound of formula I to a CCK receptor" and the specification provides that the compounds are appetite suppression agents, antiulcer agents, etc. (see pages 33-39). The phrase "a condition advantageously affected", however, is not fully understood and further, the instant recitation reads on all types of conditions that are known to exist and those that may be discovered in future. The specification did not provide any competent tests or data to establish that the compounds have the claimed activity of being therapeutically useful in treating all types of 'conditions advantageously affected by the binding of the compound to CCK receptor'.

Claim 84 specifically recites 'a method of blocking drug or alcohol withdrawal reaction' - the scope of this claim is beyond what has been established for such a treating effect. The specification teaches that the compounds exhibit affinity for CCK receptors. However, the

notion that a compound could be effective against drug or alcohol dependencies in general is absolutely contrary to our current understanding of how such dependencies operate. There is not, and probably never will be, a pharmacological treatment for "drug or alcohol withdrawal reaction" generally. That is because "drug or alcohol withdrawal reaction" is not a single disease or cluster of related disorders, but in fact, a collection with relatively little in common. Addiction to various drugs or alcohol, e.g., barbiturates, alcohol, cocaine, opiates, amphetamines, benzodiazepines, nicotine, etc. all involve different parts of the CNS system; different receptors in the body. For example, cocaine binds at the dopamine reuptake transmitter. Heroin addiction, for example, arises from binding at the opiate receptors, cigarette addiction arises from some interaction at the nicotinic acid receptors, many tranquilizers involve the benzodiazepine receptor, alcohol involves yet another system, etc. All attempts to find a pharmaceutical to treat drug or alcohol withdrawal reaction generally have thus failed.

Further, claim 87 recites 'a method of diagnosis of gastrin-dependent tumors' and the specification does not provide how this method is accomplished. The test procedures and the activity data discussed in the specification related to CCK binding does not provide any nexus to the instantly recited method of use. Further, there is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. Note *In re Surrey*, 151 USPQ 724 regarding sufficiency of disclosure for a Markush group.

There is no disclosure regarding how 'the mammal in need of the claimed therapeutic activity' is identified and further, how all types of therapeutic uses are achieved. See MPEP §

2164.03 for enablement requirements in cases directed to structure-specific arts such as the pharmaceutical art. Receptor activity is generally unpredictable and highly structure specific area, and the data provided of the single compound is insufficient for one of ordinary skill in the art in order to extrapolate to the other compounds of the claims. It is inconceivable as to how the diagnosis of the gastrin-dependent tumors is carried out and the specification does not provide any procedures or examples to establish the use of radiolabelled iodo compounds of formula I.

There is no evidence of record which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease(s) or disorder(s) claimed herein and therefore, require the treatment and/or diagnosis. Next, applicant's attention is drawn to the Revised Interim Utility and Written Description Guidelines, at 64 FR 71427 and 71440 (December 21, 1999) wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed 'treating a condition advantageously affected by binding of CCK receptor' solely based on the activity data disclosed for the compounds.

Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(Only a few of the claimed diseases are discussed here to make the point of an insufficient disclosure, it does not definitely mean that the other diseases meet the enablement requirements).

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 74 and 79 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

- Claim 74 recites the limitation "A pharmaceutically acceptable salt of claim 73" in lines 1-2. There is insufficient antecedent basis for this limitation in claim 73 on which claim 74 is dependent. Claim 73 does not recite 'pharmaceutically acceptable salt of a compound of formula I'.

- In claim 79, the recitation "a condition advantageously affected by the binding of the compound of Formula I to a CCK receptor" is not fully understood. It is not clear what 'conditions' are intended by the recitation.

Allowable Subject Matter

Claims 76, 77, 80-83, 85 and 86 are allowed. The references of record do not teach or fairly suggest the claimed compounds.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Mukund Shah, can be reached on (571) 262-0674. If you are unable to reach Dr. Shah within a 24 hour period, please contact James O. Wilson, Acting-SPE of 1624 at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deepak Rao
Primary Examiner
Art Unit 1624

July 25, 2004